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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 06/03/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/520,130

Applicant(s)

ARATHOON ET AL.

Examiner

Anne Holleran

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 13 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 12-14, 16-18 and 34-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-14, 16-18 and 34-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage

a) ☐ The translation of the foreign language provisional application has been received

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- ☐ Information Disclosure Statement(s) (PTO Form 1449 Paper No. 1)
- ☐ Other

### DETAILED ACTION

1. The amendment filed March 14, 2003 is acknowledged. Claims 31 and 33 were canceled. Claims 39-47 were added. Claim 14 was amended.

Claims 12-14, 16-18, and 34-47 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections Maintained and New Grounds of Rejection:***

3. The rejection of claims 12-14, 16-18, and 34-38 under 35 U.S.C. 112, first paragraph, on the grounds that the specification is not enabling for the full scope of the claimed inventions is maintained. This rejection is applied to new claims 39-47.

The claims are drawn to bispecific antibodies comprising 2 polypeptides, where each polypeptide comprises a heavy chain, light chain and multimerization domain. The light chain of each of the two polypeptides may be identical because the claims recite that either the first or the second polypeptide comprises either a first or second light chain. The first and second light chains must be at least 80 percent identical to each other. Because of the way the claims are drawn, the first and second polypeptides may both comprise the first light chain, or both other may comprise the second light chain.

Applicant's arguments are unpersuasive, because they fail to demonstrate where in the specification support may be found for methods for specifically altering the sequences of the first or second light chain to arrive at sequences that are at least 80 percent identical, but still may be interchangeably used to bind with either of the two heavy chains to make a bispecific antibody. Furthermore, even though the specification generally contemplates bispecific antibodies where each binding domain of the bispecific antibody comprises a different light chain where the two light chains are at least 80 percent identical in sequence, the specification fails to teach how to use the bispecific antibodies that are made when the incorrect light chain binds to a heavy chain. As the claims are currently recited, either one of the two light chains may bind. Thus, the rejection is maintained for the reasons of record.

The specification confines its examples to how to screen scFv libraries to find antibody pairs that could be used in bispecific scFv constructs where the light chain is identical. The specification fails to teach how to make such bispecific antibodies, and only teaches how to screen an scFv library for the purpose of discovering heavy and light chain pairings, where one light chain binds to two different heavy chains to make a binding domain that binds to different antigens. The specification fails to teach examples where, after finding such a heavy and light chain pairings, the light chain sequence is then altered and then the altered light chain retains the ability to pair with either heavy chain and the resulting binding domains bind antigen.

As set forth in the previous office action, minor modifications in the binding domain of engineering appears to be highly unpredictable and one of skill in the art would not have a reasonable expectation for success in how to make the full scope of the claimed antibodies.

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4. The rejection of claims 12-14, 16-18, 31 and 33-38 under 35 U.S.C. 112, first paragraph, on the grounds that the applicant was not in possession of the claimed inventions at the time of filing, because the disclosure of the specification fails to adequately describe the claimed genus of compounds is maintained for the reasons of record. This rejection is applied to new claims 39-45 and 47.

Applicant's arguments are unpersuasive, because the arguments fail to show where the specification describes any examples where the light chains are not identical. In view of the broad scope of the claims and the lack of enablement (*supra*) and the lack of examples representative of the broad genus, the specification fails to provide support for the claimed genus.

Additionally, new claims 44, 45 and 47 add new matter into the specification. Thus, the basis for the rejection of the claims is two-fold. The specification fails to adequately describe the claimed genus, and for claims 44, 45 and 47, the claims introduce new matter into the specification. There does not appear to be support in the specification for the limitation that the first and second light chains 98 or 99 percent identity; or have 80 percent identity and have at least one CDR region that has the same sequence.

5. The rejection of claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite for the invention is maintained for the reasons of record. The amendment fails to correct the indefiniteness of the phrase "the original nucleic acid".

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Claim 14 is indefinite because the phrase "the original nucleic acid" lacks antecedent basis in claim 13.

7. The rejection of claims 12-14, 16-18, 34-38 under 35 U.S.C. 103(a) as being unpatentable over Vaughan (Nature Biotechnology, 14: 309-314, 1996; cited in the IDS) in view of Bosslet (U.S. Patent 5,591,828; issued Jan. 7, 1997; effective filing date of 6/20/1990) and further in view of either Ridgway (Protein Engineering, 9: 617-621, 1996), or Carter (WO 96/27011; published September 1996; cited in the IDS) is maintained. The examiner has removed the rejection over Carter (U.S. Patent 5,807,706). The rejection is applied to new claims 39-47.

Applicant's arguments are unpersuasive, because applicant argues each reference individually. The prior art as a whole suggests and teaches the claimed inventions. The teaching of Vaughan that it is possible to make two different scFvs having identical light chains paired to different heavy chains suggests the claimed inventions. The Bosslet, and Ridgeway or Carter(WO) are supplied to demonstrate that a bispecific antibody that bound to DTPA and CEA would have use; and that addition of multimerization domains are known in the art. Therefore, the prior art as a whole teaches the claimed inventions.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran  
Patent Examiner  
June 2, 2003